PATENT

Attorney Docket No. A-64260-4/DJB/RMS/AMS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	)	Examiner: Not Assigned
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NOLAN and ROTHENBERG	)	Group Art Unit: Unknown
	)	
Serial No. Unknown	)	San Francisco, California
	)	
Filed: Herewith	)	
	)	
For: METHODS FOR SCREENING FOR TRANSDOMINANT INTRA-CELLULAR EFFECTOR PEPTIDES AND RNA MOLECULES	)	"EXPRESS MAIL" MAILING LABEL NUMBER EL758643396US DATE OF DEPOSIT July 31, 2001 I HEREBY CERTIFY THAT THIS PAPER OR FEE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE "EXPRESS MAIL POST OFFICE TO ADDRESSEE" SERVICE UNDER 37 CFR 1.10 ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO: ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, DC 20231. TYPED NAME DARRYL KRINER SIGNED

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

Prior to substantive examination please amend the above-referenced application as indicated below.

The Commissioner is authorized to charge any fees including extension fees or other relief which may be required, or credit any overpayment to Deposit Account No. 06-1300 (Our Order No. A-64260-4/DJB/RMS/AMS).

In the Claims:

Please cancel claims 1-22, without prejudice or disclaimer.

Please add the following new claims:

--23. A method for in vitro screening for a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

a) introducing a molecular library of randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence, wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized peptides;

b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent; and

c) identifying said transdominant bioactive agent.

24. A method according to claim 23 wherein said identifying comprises:

i) isolating said cell exhibiting an altered phenotype; and

ii) isolating said nucleic acid encoding said transdominant bioactive agent.

25. A method according to claim 24 wherein said identifying further comprises:

iii) sequencing said nucleic acid encoding said transdominant bioactive agent.

26. A method for in vitro screening for a molecule that binds a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

a) introducing a molecular library of randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence, wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized peptides;

b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent; and

c) identifying a target molecule to which said transdominant bioactive agent binds.

27. A method according to claim 26 wherein said identifying comprises:

i) isolating said cell exhibiting an altered phenotype;

ii) isolating said transdominant bioactive agent; and

iii) binding said transdominant bioactive agent to said target.

28. A method according to claim 23 or claim 26 further comprising the step:

d) isolating a target molecule using

i) said candidate nucleic acid; or

ii) the expression product of said candidate nucleic acid.

29. A method according to claim 23 or claim 26 wherein said nucleic acids further comprise a presentation sequence capable of presenting said expression product in a conformationally restricted form.

30. A method according to claim 23 or claim 26 wherein said introducing is with retroviral vectors.

31. A method according to claim 23 or claim 26 wherein said cells are mammalian cells.

32. A method according to claim 23 or claim 26 wherein said library comprises at least 10^4 different nucleic acids.

33. A method according to claim 23 or claim 26 wherein said library comprises at least 10^5 different nucleic acids.

34. A method according to claim 23 or claim 26 wherein said library comprises at least 10^6 different nucleic acids.

35. A method according to claim 23 or claim 26 wherein said library comprises at least 10^7 different nucleic acids.

36. A method according to claim 23 or claim 26 wherein said library comprises at least 10^8 different nucleic acids.

37. A method according to claim 23 or claim 26 wherein each of said candidate nucleic acids is linked to nucleic acid encoding at least one fusion partner.

38. A method according to claim 37 wherein said fusion partner is a presentation sequence capable of presenting said expression product in a conformationally restricted form.

39. A method according to claim 37 wherein said fusion partner is a rescue sequence.

40. A method according to claim 37 wherein said fusion partner is a stability sequence.

41. A method according to claim 37 wherein said fusion partner is a dimerization sequence.

42. A method according to claim 37 wherein said fusion partner is a targeting sequence.

43. A method according to claim 42 wherein said targeting sequence is selected from the group consisting of:

a) a localizing signal sequence capable of constitutively localizing said translation product to a predetermined subcellular locale;

b) a membrane-anchoring sequence capable of localizing said translation product to a cellular membrane; and

c) a secretory signal sequence capable of effecting the secretion of said translation product.

44. A method according to claim 43 wherein said targeting sequence is a nuclear localization signal (NLS).

45. A method according to claim 43 wherein said targeting sequence is a myristylation sequence.

46. A method for in vitro screening for a transdominant bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

a) introducing a molecular library of randomized candidate nucleic acids into a first plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence;

b) contacting said first plurality of cells with a second plurality of cells;

c) screening said second plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent; and

d) identifying said transdominant bioactive agent.

47. A method according to claim 46 wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized candidate peptides.

48. A method according to claim 47 wherein each of said candidate nucleic acids is linked to a nucleic acid encoding at least one fusion partner.

49. A method according to claim 48 wherein said fusion partner is a targeting sequence comprising a secretory signal sequence capable of effecting the secretion of said candidate peptides.

50. A method for in vitro screening for a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

a) introducing a molecular library of retroviral vectors comprising randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence and wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized peptides;

b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent; and

c) identifying said transdominant bioactive agent.

REMARKS

New claims 23-50 are pending. Support for the new claims is found throughout the specification and as further described. New claim 23 is identical to issued claim 1 of U.S. Patent No. 6,153,380, (a parent of the present application), with the additional element of identifying the transdominant bioactive agent. Support for "identifying said transdominant bioactive agent" is at p. 34, lines 13-25. New claim 26 is identical to issued claim 1 of U.S. Patent No. 6,153,380, with the additional element of identifying a target molecule to which the transdominant bioactive agent binds. Support for "identifying a target molecule to which said transdominant bioactive agent binds" is at p. 35, line 13 to p. 36, line 7.

Support for new claim 24 is found at p. 34, lines 3-4 and 13-14. Support for new claim 25 is found at p. 34, lines 24-25. Support for claim 27 is found at p. 34, lines 3-4 and 13-14., and p. 35, line 19 to p.36, line 7. Claims 28-45 depend from claims 23 and 26 (or dependent claims therefrom) and further recite identical elements as in issued claims 4-12 and 14-22, respectively, of U.S. Patent No. 6,153,380. Claims 47-49 depend from claim 46 (or dependent claims therefrom) and further recite identical elements as in issued claims 24-26, respectively, of U.S. Patent No. 6,153,380. Claim 46 is identical to claim 23 of U.S. Patent No. 6,153,380, with the additional element "identifying said transdominant bioactive agent," which has support at p. 34, lines 13-25. Claim 50 is identical to claim 27 of U.S. Patent No. 6,153,380, with the additional element "identifying said transdominant bioactive agent," which has support at p. 34, lines 13-25.

Applicants respectfully submit that the claims are in condition for allowance, and an early notification of such is respectfully requested. Please direct any calls in connection with this application to the undersigned attorney.

Respectfully submitted,

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